```
 b 155, 5
      18sep02 14:01:57 User242957 Session D510.2
           $0.00    0.073 DialUnits File410
     $0.00  Estimated cost File410
     $0.00  Estimated cost this search
     $0.05  Estimated total session cost   0.386 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2002/Sep W3
*File 155: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File   5:Biosis Previews(R)  1969-2002/Sep W3
         (c) 2002 BIOSIS
*File   5: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.

      Set  Items  Description
      ---  -----  -----------
? s analyt?
      S1  575025  ANALYT?
? s s1 and nucleic?
          575025  S1
          196572  NUCLEIC?
      S2    7158  S1 AND NUCLEIC?
? s s2 and alkyl?
>>>File 5 processing for ALKYL? stopped at ALKYLNAPHTHALIMIDES
            7158  S2
           87186  ALKYL?
      S3      37  S2 AND ALKYL?
? rd
...completed examining records
      S4      35  RD (unique items)
? t s4/3,ab/all

 4/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09825702   98258062   PMID: 9595698
  Capillary electrophoretic separation of cationic porphyrins.
  Dixon D W; Pu G; Wojtowicz H
  Department of Chemistry, Georgia State University, Atlanta 30303, USA.
  Journal of chromatography. A (NETHERLANDS)  Apr 10 1998,  802  (2)
 p367-80,   Journal Code: 9318488
  Contract/Grant No.: AI127196; AI; NIAID
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Cationic porphyrins have a wide variety of uses including those as
nucleic acid binding and cleaving agents, as potential
pharmacological agents, as electron donor/acceptors in intramolecular
electron transfer processes and as analytical reagents. Herein, we
report the separation of cationic porphyrins by capillary electrophoresis
on fused silica in phosphate buffer at pH 2-5. The porphyrins studied in
this work were synthesized from alkylation of the parent
tetrapyridylporphyrin (TPyP) to give various pyridinium porphyrins. For
example, methylation of TPyP gives a mixture of the mono-, cis-di-,
trans-di-, tri- and tetramethylated porphyrins [e.g.,
5,10,15,20-tetrakis(N-methyl-4-pyridiniumyl)-21H,23H-p orphyrin, TMPyP(4)].
Capillary electrophoresis on a synthetic mixture showed separation of four
of these compounds. Mixtures after alkylation with iodopropionic acid
and bromopropylamine were also separated. The cis-di- and trimethylated
TMPyP derivatives were separated on a small preparative scale by
centrifugal partition chromatography. Capillary electrophoresis was also
```

used to separate metallo TMPyP(4) complexes including those of cobalt, copper, iron, manganese, palladium, tin, vanadium and zinc. The conformational isomers (atropisomers) of 5,10,15,20-tetrakis(N-methyl-2-pyr idiniumyl)-21H,23H-p orphyrin, TMPyP(2), were also separated. Net charge, molecular mass and molecular shape all contribute to the differential retention of cationic porphyrins under capillary electrophoresis conditions. Additional factors affecting the separations, including aggregation and protonation of the porphyrins, were probed by evaluating the separation of TMPyP(4) and its butyl and octyl analogs as a function of solution conditions. Cationic porphyrins are difficult to separate using traditional chromatographic methods; capillary electrophoresis and centrifugal partition chromatography provide excellent new techniques for separation of this class of compounds.

4/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09551804 97455584 PMID: 9309878
Caffeine-DNA interactions: biochemical investigations comprising DNA-repair enzymes and **nucleic** acid synthesis.
Tempel K; von Zallinger C
Institut fur Pharmakologie, Toxikologie und Pharmazie, Universitat Munchen, Germany.
Zeitschrift fur Naturforschung. C, Journal of biosciences (GERMANY) Jul-Aug 1997, 52 (7-8) p466-74, ISSN 0341-0382 Journal Code: 8912155
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Chicken embryo cells were treated with caffeine (0.5-8.0 mM) alone or combined with various chemical and physical DNA-and/or chromatin-interactive agents. **Analytical** procedures comprised scheduled (SDS) and unscheduled (UDS) DNA synthesis, RNA synthesis (RNS), the activities of O6-**alkylguanine**-DNA **alkyltransferase** (AT) and poly (ADP-ribose) polymerase (PARP) as well as nucleoid sedimentation. Additional investigations were done in rat thymic and splenic cells. The effect of caffeine on DNase-I activity served as an in vitro-model system. When present in the PARP-, SDS-, UDS- and RNS-assays, caffeine inhibited the corresponding tracer (14C-NAD, dT-3H, 3H-U) incorporation in a dose-dependent manner. The AT activity was slightly stimulated. At concentrations of 0.06-0.3 mM, caffeine inhibited DNase-I activity by excess substrate. No specific effects of caffeine could be shown by nucleoid sedimentation. Besides the reduced permeability of the cells to **nucleic** acid precursors, the results obtained with the PARP- and DNase-I assays give evidence for the formation of a DNA-caffeine adduct as a prominent mechanism of cellular caffeine effects including DNA repair inhibition.

4/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06376542 90070258 PMID: 2686136
[The use of soft-ionization mass-spectrometry in biochemistry]
Primenenie miagkoionizatsionnoi mass-spektrometrii v biokhimii.
Sukhodub L F
Ukrainskii biokhimicheskii zhurnal (USSR) Jul-Aug 1989, 61 (4) p16-30, ISSN 0201-8470 Journal Code: 7804246
Document type: Journal Article; Review; Review, Tutorial ; English Abstract
Languages: RUSSIAN
Main Citation Owner: NLM
Record type: Completed

Basic principles of mass spectrometry (MS) and methods of ionization are described. Methodological aspects of field ionization (FI) and field desorption (FD) MS are considered in detail. Examples are given demonstrating application of FI and FD MS as an **analytical** tool for structure analysis and identification of mono-, di- and oligosaccharides, **nucleic** acid bases, nucleosides, nucleotides, oligonucleotides, biomacromolecules (DNA, polysaccharides), microorganisms, metals in biological tissues and liquids, drugs (in particular, organophosphoric compounds) and their metabolites. The possibilities of fast atom bombardment MS in the investigation of dGuo and DNA **alkylation** by thiophosphamide are demonstrated.

4/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02312391 76163498 PMID: 1260950
The kinetics of the alkaline hydrolysis of phosphotriesters in DNA.
Shooter K V
Chemico-biological interactions (NETHERLANDS) May 1976, 13 (2) p151-63, ISSN 0009-2797 Journal Code: 0227276
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The degradation in alkali of normal DNA and DNA **alkylated** with dimethyl sulphate (DMS), N-methyl-N-nitrosourea (MNUA) and N-ethyl-N-nitrosourea (ENUA) has been investigated using **analytical** ultracentrifugation techniques. For control T7-DNA (w.st. denatured form 12.5 - 10(6) daltons) the rate of degradation at 37 degrees varies from 0.14 breaks/molecule/h in 0.1 M NaOH to 1.2 breaks/molecule/h in 0.4 M NaOH. When DNA is **alkylated** with reagents known to produce phosphotriesters addition of alkali leads to an initial rapid degradation not observed with control DNA. Ethyl phosphotriesters are hydrolysed at about half the rate of methyl phosphotriesters. Approximately one third of the methyl or ethyl phosphotriesters present hydrolyse to give breaks in the DNA chain.

4/3,AB/5 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13838643 BIOSIS NO.: 200200467464
Metal ion-catalyzed **nucleic** acid **alkylation** and fragmentation.
AUTHOR: Browne Kenneth A(a)
AUTHOR ADDRESS: (a)Gen-Probe Incorporated, 10210 Genetic Center Drive, San Diego, CA, 92121**USA E-Mail: kenb@gen-probe.com
JOURNAL: Journal of the American Chemical Society 124 (27):p7950-7962 July 10, 2002
MEDIUM: print
ISSN: 0002-7863
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: **Nucleic** acid microarrays are a growing technology in which high densities of known sequences are attached to a substrate in known locations (addressed). Hybridization of complementary sequences leads to a detectable signal such as an electrical impulse or fluorescence. This combination of sequence addressing, hybridization, and detection increases the efficiency of a variety of genomic disciplines including those that profile genetic expression, search for single nucleotide polymorphisms (SNPs), or diagnose infectious diseases by sequencing

portions of microbial or viral genomes. Incorporation of reporter molecules into **nucleic** acids is essential for the sensitive detection of minute amounts of **nucleic** acids on most types of microarrays. Furthermore, polynucleic acid size reduction increases hybridization because of increased diffusion rates and decreased competing secondary structure of the target **nucleic** acids. Typically, these reactions would be performed as two separate processes. An improvement to past techniques, termed labeling-during-cleavage (LDC), is presented in which DNA or RNA is **alkylated** with fluorescent tags and fragmented in the same reaction mixture. In model studies with 26 nucleotide-long RNA and DNA oligomers using ultraviolet/visible and fluorescence spectroscopies as well as high-pressure liquid chromatography and mass spectrometry, addition of both **alkylating** agents (5-(bromomethyl)fluorescein, 5- or 6-iodo-acetamidofluorescein) and select metal ions (of 21 tested) to **nucleic** acids in aqueous solutions was critical for significant increases in both labeling and fragmentation, with gtoreq100-fold increases in **alkylation** possible relative to metal ion-free reactions. Lanthanide series metal ions, Pb2+, and Zn2+ were the most reactive ions in terms of catalyzing **alkylation** and fragmentation. While oligonucleotides were particularly susceptible to fragmentation at sites containing phosphorothioate moieties, labeling and cleavage reactions occurred even without incorporation of phosphorothioate moieties into the RNA and DNA target molecules. In fact, LDC conditions were found in which RNA could be fragmented into its component monomers, allowing simultaneous sequencing from both the 5'- and the 3'-termini by mass spectrometry. The results can be explained by **alkylation** of the (thio)phosphodiester linkages to form less hydrolytically stable (thio)-phosphotriesters, which then decompose into 2',3'-cyclic phosphate (or 2'-phosphate) and 5'-hydroxyl terminal products. Analysis of fragmentation and **alkylation** products of Mycobacterium tuberculosis (Mtb) ribosomal RNA (rRNA) transcripts by polyacrylamide gel electrophoresis was consistent with the model studies. Building upon these results, I found that products from Mtb rRNA amplification products were processed with fluorescent reporters and metal ions in a single reaction milieu for analysis on an Affymetrix GeneChip. Mild conditions were discovered which balanced the need for aggressive **alkylation** and the need for controlled fragmentation, advantageously yielding GeneChip results with greater than 98% of the nucleotides reported correctly relative to reference sequences, results sufficient for accurately identifying Mtb from other Mycobacterium species. Thus, LDC is a new, straightforward, and rapid aqueous chemistry that is based on metal ion-catalyzed **alkylation** and **alkylation**-catalyzed fragmentation of **nucleic** acids for analysis on microarrays or other hybridization assays and that, possibly, has utility in similar processing of other appropriately functionalized biomolecules.

2002

4/3,AB/6 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13742587 BIOSIS NO.: 200200371408
Electrochemical sensor for detection of unmodified **nucleic** acids.
AUTHOR: Popovich N D(a); Eckhardt A E; Mikulecky J C; Napier M E; Thomas R S
AUTHOR ADDRESS: (a)Xanthon, Inc., 104 T.W. Alexander Drive, P.O. Box 12296, Research Triangle Park, NC, 27709**USA
JOURNAL: Talanta 56 (5):p821-828 1 April, 2002
MEDIUM: print
ISSN: 0039-9140
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have developed a **nucleic** acid (NA) sensor based on mediated electrochemical oxidation of guanine residues. In this method, oligonucleotide probes are bound to a tin-doped indium oxide (ITO) electrode through a self-assembled phosphonate monolayer. The end carboxyl moiety of the monolayer is activated with carbodiimide and reacted with the amine group of a C6 **alkyl** linker which has been added to the 5'-end of the oligonucleotide probe. Upon hybridization of the complementary target NA, the hybrid is detected using a redox-active mediator, tris(2,2'-bipyridyl) ruthenium(II). We speculate that the monolayer does not impede electron-transfer since it contains many defect sites when assembled on a polycrystalline ITO surface. These defect sites are accessible to the mediator, but not to NA or proteins. The electrocatalytic current was a linear function of the amount of guanine bound at the electrode surface, with a detection limit of 120 amoles of guanine cm-2 at 0.28 cm2 ITO electrodes.

2002

4/3,AB/7 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13640900 BIOSIS NO.: 200200269721
The modulation by xanthines of the DNA-damaging effect of polycyclic aromatic agents. Part II. The stacking complexes of caffeine with doxorubicin and mitoxantrone.
AUTHOR: Piosik Jacek; Zdunek Malgorzata; Kapuscinski Jan(a)
AUTHOR ADDRESS: (a)Intercollegiate Faculty of Biotechnology, Department of Molecular and Cellular Biology, Laboratory of Biophysical Chemistry, University of Gdansk and Medical University of Gdansk, Kladki 24, 80-822, Gdansk**Poland E-Mail: jankap biotech.univ.gda.pl
JOURNAL: Biochemical Pharmacology 63 (4):p635-646 15 February, 2002
MEDIUM: print
ISSN: 0006-2952
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Recently accumulated statistical data indicate the protective effect of caffeine consumption against several types of cancer diseases. There are also reports about protective effect of caffeine and other xanthines against tumors induced by polycyclic aromatic hydrocarbons. One of the explanations of this phenomenon is based on biological activation of such carcinogens by cytochromes that are also known for metabolism of caffeine. In the accompanying paper (Kapuscinski et al., this issue) we provide evidence (flow cytometry and the cell cycle analysis) that the cytostatic effects of caffeine (CAF) on two DNA **alkylating** agents, which do not require the biological activation, depend on their ability to form stacking (pi-pi) complexes. In this study, we use physicochemical techniques (computer aided light absorption and microcalorimetry), and molecular modeling to examine previously published qualitative data. This is published both by our and other group's data, indicates that CAF is able to modify the cytotoxic and/or cytostatic action of the two well known antitumor drugs doxorubicin (DOX) and mitoxantrone (MIT). To obtain the quantitative results from the experimental data we used the statistical-thermodynamical model of mixed aggregation, to find the association constants KAC of the CAF-drug interaction (128 +- 10 and 356 +- 21 M-1 for DOX-CAF and MIT-CAF complex formation, respectively). In addition, the favorable enthalpy change of CAF-MIT (DELTAH = -11.3 kcal/mol) was measured by microcalorimetry titration. The molecular

modeling (semi-empirical and force field method) allowed us to obtain the geometry of these complexes, which indicated the favorable energy (DELTAE) of complex formation of the protonated drug's molecules in aqueous environment (-7.4 and -8.7 kcal/mol for DOX-CAFcntdot5H2O and MIT-CAFcntdot8H2O complex, respectively). The molecular modeling calculation indicates the existence of CAF-drug complexes in which the MIT molecules are intercalated between two CAF molecules (DELTAE = -29.9 kcal/mol). These results indicate that the attenuating effect of caffeine on cytotoxic or mutagenic effects of some polycyclic aromatic mutagens cannot be the result of metabolic activation in the cells, but simply is the physicochemical process of the sequestering of aromatic molecules (e.g. carcinogens or mutagens) by formation of the stacking complexes. The caffeine may then act as the "interceptor" of potential carcinogens (especially in the upper part of digesting track) where its concentration can reach the mM level). There is, however, no indication, both, in the literature or from our experiments, that the xanthines can reverse the damage to **nucleic** acids at the point when the damage to DNA has already occurred.

2002

4/3,AB/8 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13640899 BIOSIS NO.: 200200269720
The modulation of the DNA-damaging effect of polycyclic aromatic agents by xanthines. Part I. Reduction of cytostatic effects of quinacrine mustard by caffeine.
AUTHOR: Kapuscinski Jan(a); Ardelt Barbara; Piosik Jacek; Zdunek Malgorzata ; Darzynkiewicz Zbigniew
AUTHOR ADDRESS: (a)Laboratory of Biophysical Chemistry, Department of Molecular and Cellular Biology, Intercollegiate Faculty of Biotechnology, University of Gdansk and Medical University of Gdansk, Kladki 24, 80-822, Gdansk**Poland E-Mail: jankap@biotech.univ.gda.pl
JOURNAL: Biochemical Pharmacology 63 (4):p625-634 15 February, 2002
MEDIUM: print
ISSN: 0006-2952
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Recently, accumulated statistical data indicate the protective effect of caffeine consumption against several types of cancer diseases. There are also reports about protective effect of caffeine and other xanthines against tumors induced by polycyclic aromatic hydrocarbons. One of the explanations is based on biological activation of such carcinogens by cytochromes that are also known for metabolism of caffeine. However, there is also numerous data indicating reverse effect on cytotoxicity of anticancer drugs that inhibit the action of topoisomerase I (e.g. Camptothecin or Topotecan) and topoisomerase II inhibitors (e.g. Doxorubicin, Mitoxantrone or mAMSA). In this work we tested the hypothesis that the caffeine protective effect is the result of sequestering of aromatic mutagens by formation of stacking (pi-pi) complexes. As the models for the study we have chosen two well-known mutagens, that do not require metabolical activation: quinacrine mustard(QM, aromatic, heterocyclic nitrogen mustard) and mechlorethamine (NM2, aliphatic nitrogen mustard). The flow cytometry study of these agents' action on the cell cycle HL-60 cells indicated that caffeine prevents the cytotoxic action of QM, but not that of NM2. The formations of stacking complexes of QM with caffeine were confirmed by light absorption, calorimetric measurements and by molecular modeling calculation. Using the statistical thermodynamics calculations we

calculated the "neighborhood" association constant (KAC = 59 +- 2 M-1) and enthalpy change (DELTAH0' = -116 cal mol-1); the favorable entropy change of complex formation (DELTAS0' = 7.72 cal mol-1 K-1, due to release of several water molecules, associated with components in the process of complex formation). The Gibbs' free energy change of QM-CAF formation is DELTAG0' = -2.41 kcal mol-1. We were unable to detect any interaction between NM2 and caffeine either by spectroscopic or calorimetric measurement. In order to establish, whether the intercalation of QM plays any role in cytotoxic effect we tested, as a control, non-**alkylatiatig**, but also intercalating QM derivative-quinacrine (Q). The later had no cytostatic effect on HL-60 cell even at there order of higher concentration than QM or NM2 but, similar to QM forms (which we demonstrated) stacking complexes with caffeine (KAC = 75 +- 3 M-1). These results strongly indicate, that the attenuating effect of caffeine on cytotoxic or mutagenic effects of some mutagens, is not the results of metabolic processes in the cells, but simply the physicochemical process of sequestering of aromatic molecules (potential carcinogens or mutagens) by formation of stacking complexes with them. The caffeine may then act as the "interceptor" of potential carcinogens (especially in the upper part of digesting track where its concentration can reach the concentration of mM level). There is, however, no indication either in the literature or in our experiments that xanthines can reverse the damage to **nucleic** acids when the damage to DNA has already occurred.

2002

4/3,AB/9 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13522954 BIOSIS NO.: 200200151775
INACTINETM PEN110 mechanism of action: Disruption of **nucleic** acid replication.
AUTHOR: Golitsina Nina(a); McKenzie Andres(a); Purmal Andrei(a)
AUTHOR ADDRESS: (a)V.I. Technologies, Inc, Watertown, MA**USA
JOURNAL: Blood 98 (11 Part 2):p105b November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 2 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The INACTINETM process for improving the pathogen safety of red blood cell concentrates (RBCCs) involves incubation with 0.1% (v/v) PEN110 (a proprietary chemical INACTINETM agent) at 23degreeC for 24 h, followed by automated washing of RBC. PEN110 is a small electrophilic compound with broad-spectrum antiviral (non-enveloped and enveloped) and antibacterial activities and is thought to inhibit replication of infectious organisms by modification of their genomes. The PEN110 molecule is comprised of two functional domains, a substituted **alkyl** chain bearing positive charges and an aziridino group, which **alkylates** nucleophiles when protonated. The selectivity of PEN110 for nucleophilic centers of **nucleic** acids (NA) is attributed to a proposed three-step enzyme-like chemical reaction: 1) initial ionic binding of positively-charged PEN110 to negatively-charged internucleotide phosphate groups; 2) in situ self-activation of PEN110's aziridino group by protonation and 3) covalent modification (**alkylation**) of neighboring nucleophilic groups (predominantly N7 of guanine) by the activated PEN110. N7 Guanine **alkylation** can cause opening of the imidazole ring, base loss and strand breaks, resulting in disruption of transcription and replication of the pathogen genome. Model

NA (ss and ds M13 DNA, F-tRNA) were incubated with 0.1% (v/v) PEN110 at 23degreeC for 24 h in: 1) MOPS buffer, pH 7.0, 0-500 mM NaCl or KCl; 2) Na-phosphate buffer, pH 6.0-8.0 or 3) MOPS buffer, pH 7.0 containing 25% human CPD/AS-1 supplemented plasma. Aliquots were removed during the incubation and analyzed by gel electrophoresis followed by staining with EtBr. For the replication experiment, PEN110-treated ss M13 DNA was purified by gel filtration, annealed to 5'-32P labeled primer and used as a template to DNA polymerase. Primer extension products were analyzed by gel electrophoresis. Incubation with PEN110 caused exposure time, ionic strength and pH dependent fragmentation of NA. Human plasma or type of cation (Na+ or K+) had no effect on the rate of degradation. Although ds M13 DNA and F-tRNA showed slower rates of fragmentation compared to ss M13 DNA, no intact NA were detected after 24 hr of incubation under buffer conditions similar to physiological (pH 7-7.5, salt concentration apprx150 mM). In the primer extention study, PEN110 treatment of M13 DNA resulted in appearance of DNA bands truncated at the sites, most of which corresponded to guanine in the template strand. Increased ionic strength during PEN110 treatment resulted in a greater degree of primer extention regardless of the type of cation used. No full size DNA copy was detected using the template strand treated with PEN110 under buffer conditions similar to physiological. PEN110 covalently modifies NA as demonstrated by the observed patterns of fragmentation. The reduced extent of fragmentation at high ionic strength and pH is in agreement with the proposed mechanism of action. NA secondary structure slows down but doesn't prevent degradation, and plasma proteins have no effect on the interaction of PEN110 with NA. The replication study confirms that guanine is the preferred target base for PEN110's attack on DNA. These results strongly support the proposition that PEN110 inhibits replication of infectious organisms by covalent modification of their genome.

2001

4/3,AB/10 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13414041 BIOSIS NO.: 200200042862
Methods and compounds for labeling DNA with xanthine and lower **alkyl** substituted xanthine derivatives and reagents for the in situ detection of chromosomes
AUTHOR: Cruickshank K A; Taron D J
AUTHOR ADDRESS: Naperville, Ill.**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1185 (5):p3480 April 30, 1996
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Citation
LANGUAGE: English
1996

4/3,AB/11 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13161072 BIOSIS NO.: 200100368221
Peroxiredoxin in bovine ocular tissues: Immunohistochemical localization and in situ hybridization.
AUTHOR: Singh Aruna K; Shichi Hitoshi(a)
AUTHOR ADDRESS: (a)Department of Ophthalmology, Wayne State University School of Medicine, Detroit, MI, 48201: hshichi@med.wayne.edu**USA
JOURNAL: Journal of Ocular Pharmacology and Therapeutics 17 (3):p279-286 June, 2001

MEDIUM: print
ISSN: 1080-7683
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Peroxiredoxins are widely distributed in nature and constitute a molecular family of antioxidant enzymes which decompose hydrogen peroxide and **alkyl** hydroperoxides. We have previously characterized a peroxiredoxin from bovine ciliary body and deduced its amino acid sequence from analysis of cDNA clones encoding the protein. In this work, we investigated the immunolocalization of this novel antioxidant enzyme and its mRNA expression in bovine eye tissues. High levels of immunoreactivity and mRNA for the enzyme were detected in corneal epithelium. Distinct immunoreactivity and mRNA expression for peroxiredoxin were also detected in uveal tissues, some of the retinal cell layers and ocular vasculature.

2001

4/3,AB/12 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13135437 BIOSIS NO.: 200100342586
Ethidium bromide and SYBR Green I enhance the genotoxicity of UV-irradiation and chemical mutagens in E. coli.
AUTHOR: Ohta Toshihiro(a); Tokishita Shin-ichi; Yamagata Hideo
AUTHOR ADDRESS: (a)School of Life Science, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo, 192-0392: ohta@ls.toyaku.ac.jp**Japan
JOURNAL: Mutation Research 492 (1-2):p91-97 31 May, 2001
MEDIUM: print
ISSN: 0027-5107
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Ethidium bromide (EtBr) and SYBR Green I are **nucleic** acid gel stains and used commonly in combination with UV-illumination. EtBr preferentially induces frameshift mutations but only in the presence of an exogenous metabolic activation system, while SYBR Green I is a very weak mutagen that induces frameshift mutations. We found that EtBr and SYBR Green I, without an added metabolic activation system, strongly potentiated the base-substitution mutations induced by UV-irradiation in E. coli B/r WP2 cells. Each DNA stain alone showed no mutagenicity to the strain. Base-substitutions induced by 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone (MX) and 4-nitroquinoline-1-oxide were similarly potentiated by EtBr and SYBR Green I. SYBR Green I had a much greater effect. No enhancing effects were observed on mutations induced by mitomycin C, cisplatin, transplatin, cumene hydroperoxide, base analogs, and **alkylating** agents. Another DNA stain, acridine orange, showed similar enhancing effects on UV- and MX-mutagenicity, but no effect was observed for 4',6-diamidino-2-phenylindole (DAPI). UV- and MX-induced mutations in E. coli WP2s (uvrA), which is defective in nucleotide excision repair activity, were not potentiated by the addition of EtBr, SYBR Green I, or acridine orange. Those **nucleic** acid stains might inhibit the nucleotide excision repair of DNA damaged by UV and MX treatment.

2001

4/3,AB/13 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13034890 BIOSIS NO.: 200100242039
Shift in FTIR spectrum patterns in methomyl-exposed rat spleen cells.
AUTHOR: Suramana Teerayut; Sindhuphak Ratana; Dusitsin Nikorn; Posayanonda Tipicha; Sinhaseni Palarp(a)
AUTHOR ADDRESS: (a)Pesticide Safe Use Unit and Department of Pharmacology, Faculty of Pharmaceutical Sciences, and The Institute of Health Research, Chulalongkorn University, Bangkok, 10330: spalarp@chula.ac.th**Thailand
JOURNAL: Science of the Total Environment 270 (1-3):p103-108 10 April, 2001
MEDIUM: print
ISSN: 0048-9697
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Methomyl is a highly toxic carbamate insecticide which is widely used in many agricultural countries. We have applied the Fourier-transformed infrared (FTIR) spectroscopic method to study the toxicity of methomyl on cytoskeletal protein and the **nucleic** acid of rat spleen cells. Rats were given methomyl by gavage at 2, 6 and 8 mg/kg in single doses. Colchicine, a microtubule-disrupting agent, was given to rats at 2, 4, and 6 mg/kg in single doses and mitomycin C, an **alkylating** agent which acts as a DNA-cross-linking agent, was given by an intraperitoneal route to rats at 1 mg/kg. It was shown that the wavenumber of FTIR spectra at amide I and amide II in both methomyl- and colchicine-exposed rats shifted in dose response manner when compared with the control ($P < 0.05$). The amide I and II shifts in these regions have been proposed to be the result of an alpha-helix protein conformational change. Toxic doses of mitomycin C, a DNA-cross-linking agent, did not result in this pattern. Moreover, all exposed rats showed an increase in the absorbance ratios that were related to the vibrational mode of the phosphodiester group in **nucleic** acid ($P < 0.05$).

2001

4/3,AB/14 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12985691 BIOSIS NO.: 200100192840
Crystal structure of the catalytic core component of the **alkylhydroperoxide** reductase AhpF from Escherichia coli.
AUTHOR: Bieger Boris; Essen Lars-Oliver(a)
AUTHOR ADDRESS: (a)Department of Membrane Biochemistry, Max-Planck-Institute for Biochemistry, Am Klopferspitz 18a, D-82152, Martinsried: essen@biochem.mpg.de**Germany
JOURNAL: Journal of Molecular Biology 307 (1):p1-8 16 March, 2001
MEDIUM: print
ISSN: 0022-2836
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: **Alkylhydroperoxide** reductases (AhpR, EC 1.6.4.*) are essential for the oxygen tolerance of aerobic organisms by converting

otherwise toxic hydroperoxides of lipids or **nucleic** acids to the corresponding alcohols. The AhpF component belongs to the family of pyridine nucleotide-disulphide oxidoreductases and channels electrons from NAD(P)H towards the AhpC component which finally reduces cognate substrates. The structure of the catalytic core of the Escherichia coli AhpF (A212-A521) with a bound FAD cofactor was determined at 1.9 ANG resolution in its oxidized state. The dimeric arrangement of the AhpF catalytic core and the predicted interaction mode between the N-terminal PDO-like domain and the NADPH domain favours an intramolecular electron transfer between the two redox-active disulphide centres of AhpF.

2001

4/3,AB/15 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12886357 BIOSIS NO.: 200100093506
A new strategy of discrimination of a point mutation by tandem of short oligonucleotides.
AUTHOR: Pyshnyi D V(a); Lokhov S G(a); Podyminogin M A(a); Ivanova E M(a); Zarytova V F(a)
AUTHOR ADDRESS: (a)Novosibirsk Institute of Bioorganic Chemistry, Lavrentjev prosp., 8, Novosibirsk, 630090**Russia
JOURNAL: Nucleosides Nucleotides & Nucleic Acids 19 (10-12):p1931-1941 October-December, 2000
MEDIUM: print
ISSN: 1525-7770
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: A new strategy based on the use of cooperative tandems of short oligonucleotide derivatives (TSOD) has been proposed to discriminate a "right" DNA target from a target containing a single nucleotide discrepancy. Modification of a DNA target by oligodeoxyribonucleotide reagents was used to characterize their interaction in the perfect and mismatched complexes. It is possible to detect any nucleotide changes in the binding sites of the target with the short oligonucleotide reagent. In the presence of flanking di-3',5'-N-(2-hydroxyethyl)phenazinium derivatives of short oligonucleotides (effectors) the tetranucleotide **alkylating** reagent modifies DNA target efficiently and site-specifically only in the perfect complex and practically does not modify it in the mismatched complex. It has been shown that TSOD is much more sensitive tool for the detection of a point mutation in DNA as compared to a longer oligonucleotides.

2000

4/3,AB/16 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12534778 BIOSIS NO.: 200000288280
Determination of the structural role of the linking moieties in the DNA binding of adozelesin.
AUTHOR: Cameron Lind; Thompson Andrew S
AUTHOR ADDRESS: (a)Department of Pharmacy and Pharmacology, University of Bath, Claverton Down, Bath, BA2 7AY**UK
JOURNAL: Biochemistry 39 (17):p5004-5012 May 2, 2000
MEDIUM: print.

ISSN: 0006-2960
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Adozelesin (formerly U73975, The Upjohn Co.) is a monofunctional DNA **alkylating** analogue of the antitumor antibiotic (+)-CC-1065. Adozelesin consists of a cyclopropa(c)pyrrolo(3,2-e)indol-4(5H)-one (CPI) **alkylating** subunit of (+)-CC-1065 and a indole and benzofurans subunit replacing the more complex pyrroloindole B and C subunits, respectively, of (+)-CC-1065. Previous studies have shown that adozelesin forms a reversible covalent DNA duplex adduct via a reaction between the N3 of adenine and the cyclopropyl of the cyclopropapyrroloindole (CPI) subunit. Gel electrophoresis studies have shown that adozelesin, like all the monofunctional (CPI)-based antitumor antibiotics, has a sequence preference for 5'-TTA*-3' (the asterisk (*) indicates covalently modified base). Molecular-modeling studies have shown that the bound adozelesin ligand spans a total of five base pairs including the modified adenine. These studies have also indicated that, owing to the orientation of the ligand within the base minor groove, there should be an overall preference for sequences rich in AcntdotT base pairs, thus avoiding steric crowding around the exocyclic NH2 of any guanines present. In this study, we have prepared and studied, by high-field NMR and restrained molecular mechanics (rMM) and dynamics (rMD), the duplex adduct formed between adozelesin and 5'-CGTAAGCGCTTA*CG-3'. Previous molecular-modeling studies suggested that this sequence should be less preferred, since the two GC base pairs should lead to extensive steric crowding within the adduct, and this hypothesis has, however, never been supported by DNA-footprinting data. 1H NMR of the adozelesin duplex adduct has reveals that, although Watson-Crick base pairing is maintained throughout the DNA duplex, there is significant distortion around the central base pairs. This distortion is the result of strong hydrogen-bonding between the amide linker of the indole and benzofuran subunits, and the carbonyl of a central thymine base and second, weaker, hydrogen bond to the exocyclic NH2 of the central guanine was also observed. 1H NMR and rMD also indicate that, to accommodate this hydrogen-bond system, the bound adozelesin is not positioned centrally within the minor groove but pushed toward the modified DNA strand. Previous studies on the dimeric CPI analogue bizelesin have indicated the important role the ureylene linker plays in the DNA binding. This study indicates that a similar situation exists in the reaction of adozelesin with double-stranded DNA and provides a possible explanation into the unpredicted sequence selectivity of these ligands.

2000

4/3,AB/17 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12366996 BIOSIS NO.: 200000120498
Flow cytometric analysis of a marine LAS-degrading consortia.
AUTHOR: Lopez-Amoros R; Comas J; Garcia M T; Vives-Rego J(a)
AUTHOR ADDRESS: (a)Departament de Microbiologia, Universitat de Barcelona, Av. Diagonal 645, 08028, Barcelona**Spain
JOURNAL: Microbios 101 (398):p23-36 2000
ISSN: 0026-2633
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The specific **nucleic** acid fluorochrome SYTO-13 was used in flow cytometric analysis to assess changes in the density and heterogeneity of marine bacterial populations which biodegrade linear **alkylbenzene** sulphonate (LAS). Seawater samples with LAS and incubated in the laboratory (20degreeC, 100 rpm, 30 days) were used to monitor LAS-degrading consortia. Flow cytometric studies and culture methods were used to characterize the LAS degrading bacterioplankton consortia. Fluorescence and scatter signals enabled us to define three regions (R1, R2 and R3) in the dual parameter cytograms. The distribution of the bacterial counts in these regions allowed us to monitor the formation and evolution of the consortia.

2000

4/3,AB/18 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12334684 BIOSIS NO.: 200000088186
Crystallization and preliminary X-ray analysis of the catalytic core of the **alkylhydroperoxide** reductase component AhpF from Escherichia coli.
AUTHOR: Bieger Boris; Essen Lars-Oliver(a)
AUTHOR ADDRESS: (a)Department of Membrane Biochemistry, Max-Planck-Institute for Biochemistry, Am Klopferspitz 18a, D-82152, Martinsried bei Muenchen**Germany
JOURNAL: Acta Crystallographica Section D Biological Crystallography 56 (1):p92-94 Jan., 2000
ISSN: 0907-4449
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: **Alkylhydroperoxide** reductases (AhpR, E.C. 1.6.4.chi) are essential for the oxygen tolerance of aerobic organisms, converting otherwise toxic hydroperoxides of lipids or **nucleic** acids to their corresponding alcohols. The AhpF component (521 amino-acid residues, 56.2 kDa) belongs to the family of pyridine nucleotide-disulfide oxidoreductases and channels electrons from NAD(P)H via a series of disulfides towards the AhpC component, which finally reduces the hydroperoxide substrates. Crystals of the proteolytically truncated AhpF component (residues Asn208-Ala521) of the **alkyl** hydroperoxide reductase from Escherichia coli were grown under oxidizing conditions. The crystals belong to space group P3221, with unit-cell parameters a = 60.4, c = 171.8 ANG. X-ray diffraction data were collected to 1.9 ANG resolution using synchrotron radiation. A molecular-replacement solution was found using the structure of thioredoxin reductase from Arabidopsis thaliana as a search model.

2000

4/3,AB/19 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12159822 BIOSIS NO.: 199900454671
Alkylation of **nucleic** acid components with ethylenimine and its derivatives. IV. **Alkylation** of homopolynucleotides and DNA.
AUTHOR: Voloshchuk T P(a); Patskovskii Yu B; Potopalskii A I
AUTHOR ADDRESS: (a)Institute of Molecular Biology and Genetics, Ukrainian Academy of Sciences, ul. Zabolotnogo 150, Kiev, 252143**Ukraine
JOURNAL: Bioorganicheskaya Khimiya 25 (6):p464-473 June, 1999

ISSN: 0132-3423
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Russian; Non-English
SUMMARY LANGUAGE: English; Russian

ABSTRACT: **Alkylation** of homopolynucleotides and DNA by thioTEPA and monoaziridine diethyl phosphate was studied. The modification affected **nucleic** bases and terminal phosphate groups but not internucleotide phosphate groups. It was shown that the main center of modification in poly(A) was the N1 atom, whereas the products of N6-and N3-**alkylations** were formed in smaller amounts. In poly(G), the **alkylation** proceeded predominantly at the N7 and, insignificantly, at the N1 atom of guanine; the pyrimidine N3 atom is **alkylated** poorly in poly(C) and even worse in poly(U). In the case of DNA, the major **alkylated** sites are the guanine N7 and the adenine N3; this results in DNA denaturation and the subsequent formation of products modified at N1 and N6 of adenine, N1 of guanine, and N3 of cytosine. An increase in the pH and ionic strength of the solution as well as the DNA denaturation decrease the reaction rate, whereas ultrasonic fragmentation enhances it. Upon **alkylation**, melting temperatures decrease, CD and UV spectra change, and DNA luminescence appears. To separate the reaction mixtures and identify the DNA **alkylation** products, chemical hydrolysis, ion-exchange and reverse-phase HPLC, and UV spectroscopy were used.

1999

4/3,AB/20 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12154920 BIOSIS NO.: 199900449769
Novel cationic amphiphiles as delivery agents for antisense oligonucleotides.
AUTHOR: DeLong R K; Yoo Hoon; Alahari S K; Fisher M; Short S M; Kang S H; Kole R; Janout V; Regan S L; Juliano R L(a)
AUTHOR ADDRESS: (a)Department of Pharmacology, University of North Carolina, Chapel Hill, NC, 27599**USA
JOURNAL: Nucleic Acids Research 27 (16):p3334-3341 Aug. 15, 1999
ISSN: 0305-1048
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: There has been great interest recently in therapeutic use of **nucleic** acids including genes, ribozymes and antisense oligonucleotides. Despite recent improvements in delivering antisense oligonucleotides to cells in culture, **nucleic** acid-based therapy is still often limited by the poor penetration of the **nucleic** acid into the cytoplasm and nucleus of cells. In this report we describe **nucleic** acid delivery to cells using a series of novel cationic amphiphiles containing cholic acid moieties linked via **alkylamino** side chains. We term these agents 'molecular umbrellas' since the cationic **alkylamino** chains provide a 'handle' for binding of **nucleic** acids, while the cholic acid moieties are likely to interact with the lipid bilayer allowing the highly charged **nucleic** acid backbone to traverse across the cell membrane. Optimal gene and oligonucleotide delivery to cells was afforded by a derivative (amphiphile 5) containing four cholic acid moieties. With this amphiphile used as a constituent in cationic liposomes, a 4-5 log increase in reporter gene delivery was measured. This amphiphile used alone provided

a 250-fold enhancement of oligonucleotide association with cells as observed by flow cytometry. A substantial fraction of cells exposed to complexes of amphiphile 5 and fluorescent oligonucleotide showed nuclear accumulation of the fluorophore. Enhanced pharmacological effectiveness of antisense oligonucleotides complexed with amphiphile 5 was observed using an antisense splicing correction assay that activates a Luciferase reporter. Intracellular delivery, nuclear localization and pharmacological effectiveness of oligonucleotides using amphiphile 5 were similar to those afforded by commercial cytofectins. However, in contrast to most commercial cytofectins, the umbrella amphiphile showed substantial delivery activity even in the presence of high concentrations of serum.

1999

4/3,AB/21 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12101824 BIOSIS NO.: 199900396673
Chemical and mutagenic investigations of fatty acid amide hydrolase: Evidence for a family of serine hydrolases with distinct catalytic properties.
AUTHOR: Patricelli Matthew P; Lovato Martha A; Cravatt Benjamin F(a)
AUTHOR ADDRESS: (a)10550 N. Torrey Pines Rd, La Jolla, CA, 92037**USA
JOURNAL: Biochemistry 38 (31):p9804-9812 Aug. 3, 1999
ISSN: 0006-2960
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Fatty acid amide hydrolase (FAAH) is a membrane-bound enzyme responsible for the catabolism of neuromodulatory fatty acid amides, including anandamide and oleamide. FAAH's primary structure identifies this enzyme as a member of a diverse group of **alkyl** amidases, known collectively as the "amidase signature family". At present, this enzyme family's catalytic mechanism remains poorly understood. In this study, we investigated the catalytic features of FAAH through mutagenesis, affinity labeling, and steady-state kinetic methods. In particular, we focused on the respective roles of three serine residues that are conserved in all amidase signature enzymes (S217, S218, and S241 in FAAH). Mutation of each of these serines to alanine resulted in a FAAH enzyme bearing significant catalytic defects, with the S217A and S218A mutants showing 2300- and 95-fold reductions in kcat, respectively, and the S241A mutant exhibiting no detectable catalytic activity. The double S217A:S218A FAAH mutant displayed a 230 000-fold decrease in kcat, supporting independent catalytic functions for these serine residues. Affinity labeling of FAAH with a specific nucleophile reactive inhibitor, ethoxy oleoyl fluorophosphonate, identified S241 as the enzyme's catalytic nucleophile. The pH dependence of FAAH's kcat and kcat/Km implicated a base involved in catalysis with a pKa of 7.9. Interestingly, mutation of each of FAAH's conserved histidines (H184, H358, and H449) generated active enzymes, indicating that FAAH does not contain a Ser-His-Asp catalytic triad commonly found in other mammalian serine hydrolytic enzymes. The unusual properties of FAAH identified here suggest that this enzyme, and possibly the amidase signature family as a whole, may hydrolyze amides by a novel catalytic mechanism.

1999

4/3,AB/22 (Item 18 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

11660896 BIOSIS NO.: 199800442627
Use of the 5-cyano-2,3-ditolyl tetrazolium chloride reduction test to assess respiring marine bacteria and grazing effects by flow cytometry during linear **alkylbenzene** sulfonate degradation.
AUTHOR: Lopez-Amoros Ricard; Comas Jaume; Garcia Maria Teresa; Vives-Rego Josep(a)
AUTHOR ADDRESS: (a)Dep. Microbiol., Fac. Biol., Univ. Barcelona, Av. Diagonal 645, 08028-Barcelona**Spain
JOURNAL: FEMS Microbiology Ecology 27 (1):p33-42 Sept., 1998
ISSN: 0168-6496
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Viable, total and metabolically active bacteria were determined during linear **alkylbenzene** sulfonate degradation in coastal seawater. Viable bacteria were estimated by plate counts on marine agar media while the total and metabolically active bacteria were determined with the **nucleic** acid stain SYTO-13 and the tetrazolium salt 5-cyano-2,3-ditolyl tetrazolium chloride, respectively, in double stain procedures analyzed by flow cytometry. The double stain SYTO-13/5-cyano-2,3-ditolyl tetrazolium chloride is a rapid and simple method that discriminates bacterioplankton populations according to **nucleic** acid content and formazan formation. Linear **alkylbenzene** sulfonate degradation was monitored by high-performance liquid chromatography analysis. Bacterioplankton degraded linear **alkylbenzene** sulfonate by growing to communities with a high percentage of viable and metabolically active bacteria. The bacteria produced were rapidly grazed by protozoa: however, the grazing took place mostly on metabolically active cells, which were larger than the rest of the population.

1998

4/3,AB/23 (Item 19 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11576073 BIOSIS NO.: 199800356769
Hydrophobicities of the **nucleic** acid bases: Distribution coefficients from water to cyclohexane.
AUTHOR: Shih Phoebe; Pedersen Lee G; Gibbs Paul R; Wolfenden Richard(a)
AUTHOR ADDRESS: (a)Dep. Biochem. Biophys., Univ. N.C., Chapel Hill, NC 27599-7260**USA
JOURNAL: Journal of Molecular Biology 280 (3):p421-430 July 17, 1998
ISSN: 0022-2836
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: To establish an experimental scale of hydrophobicities for the **nucleic** acid bases, comparable with a scale developed earlier for amino acid side-chains these bases and their parent compounds (purine and pyrimidin-2-one) were converted to n-butylated and tetrahydrofurylated derivatives that are appreciably soluble in cyclohexane, a truly non-polar solvent that dissolves negligible water at saturation. Distribution measurements between neutral aqueous solution and cyclohexane, at varying solute concentrations, showed no evidence of self-association of the solute in either solvent, and the possibility of specific entrainment of water by solutes entering cyclohexane was ruled

out by the results of experiments with tritiated water. In both the n-butyl and tetrahydrofuryl series, the bases span a range of -5.3 kcal mol-1 in their free energies of transfer from water to cyclohexane, and are arranged in the following rank, in order of decreasing hydrophobicity: purine > thymine > adenine > uracil > pyrimidin-2-one > hypoxanthine gtoreq cytosine gtoreq guanine. In both series of pyrimidin-2-ones, hydrophobicity decreases with introduction of an amino substituent, but addition of an exocyclic keto group results in a modest enhancement of hydrophobicity; and free energies of transfer are relatively insensitive to the position of N-**alkyl** substitution. In both series of purines, hydrophobicity decreases with the introduction of exocyclic amino and keto groups, the keto group having the greater effect; and free energies of transfer vary substantially depending on the position of N-**alkyl** 'substitution. Several additional compounds were examined to test recent predictions based on SM5.4/A, a quantum mechanical self-consistent-field solvation model; and that model was found to yield values in reasonable agreement with the experimental results.

1998

4/3,AB/24 (Item 20 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11515126 BIOSIS NO.: 199800296458
Hydrogen peroxide formation by reaction of peroxynitrite with HEPES and related tertiary amines: Implications for a general mechanism.
AUTHOR: Kirsch Michael; Lomonosova Elena E; Korth Hans-Gert; Sustmann Reiner; De Groot Herbert(a)
AUTHOR ADDRESS: (a)Inst. Physiol. Chem., Universitaetsklin. Essen, Hufelandstrasse 55, D-45122 Essen**Germany
JOURNAL: Journal of Biological Chemistry 273 (21):p12716-12724 May 22, 1998
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Organic amine-based buffer compounds such as HEPES (Good's buffers) are commonly applied in experimental systems, including those where the biological effects of peroxynitrite are studied. In such studies 3-morpholinosydnonimine N-ethylcarbamide (SIN-1), a compound that simultaneously releases nitric oxide (.NO) and superoxide (O2-.), is often used as a source for peroxynitrite. Whereas in mere phosphate buffer H2O2 formation from 1.5 mM SIN-1 was low (apprx15 muM), incubation of SIN-1 with Good's buffer compounds resulted in continuous H2O2 formation. After 2 h of incubation of 1.5 mM SIN-1 with 20 mM HEPES about 190 muM H2O2 were formed. The same amount of H2O2 could be achieved from 1.5 mm SIN-1 by action of superoxide dismutase in the absence of HEPES. The increased H2O2 level, however, could not be related to a superoxide dismutase or to a NO scavenger activity of HEPES. On the other hand, SIN-1-mediated oxidation of both dihydrorhodamine 123 and deoxyribose as well as peroxynitrite-dependent nitration of p-hydroxyphenylacetic acid were strongly inhibited by 20 mM HEPES. Furthermore, the peroxynitrite scavenger tryptophan significantly reduced H2O2 formation from SIN-1-HEPES interactions. These observations suggest that peroxynitrite is the initiator for the enhanced formation of H2O2. Likewise, authentic peroxynitrite (1 mM) also induced the formation of both O2-. d H2O2 upon addition to HEPES (400 mM)-containing solutions in a pH (4.5-7.5)-dependent manner. In accordance with previous reports it was found that at pH gtoreq5 oxygen is released in the decay of peroxynitrite. As a consequence, peroxynitrite (1 mM)-induced H2O2

formation (apprx80 mM at pH 7.5) also occurred under hypoxic conditions. In the presence of bicarbonate/carbon dioxide (20 mM/5%) the production of H2O2 from the reaction of HEPES with peroxynitrite was even further stimulated. Addition of SIN-1 or authentic peroxynitrite to solutions of Good's buffers resulted in the formation of piperazine-derived radical cations as detected by ESR spectroscopy. These findings suggest a mechanism for H2O2 formation in which peroxynitrite (or any strong oxidant derived from it) initially oxidizes the tertiary amine buffer compounds in a one-electron step. Subsequent deprotonation and reaction of the intermediate alpha-amino **alkyl** radicals with molecular oxygen leads to the formation of O2-. from which H2O2 is produced by dismutation. Hence, HEPES and similar organic buffers should be avoided in studies of oxidative compounds. Furthermore, this mechanism of H2O2 formation must be regarded to be a rather general one for biological systems where sufficiently strong oxidants may interact with various biologically relevant amino-type molecules, such as ATP, creatine, or **nucleic** acids.

1998

4/3,AB/25 (Item 21 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10803371 BIOSIS NO.: 199799424516
Human neutrophils employ the myeloperoxidase-hydrogen peroxide-chloride system to convert hydroxy-aminoacids into glycolaldehyde, 2-hydroxypropanal, and acrolein: A mechanism for the generation of highly reactive alpha-hydroxy and alpha,beta-unsaturated aldehydes by phagocytes at sites of inflammation.
AUTHOR: Anderson Melissa M; Hazen Stanley L; Hsu Fong F; Heinecke Jay W(a)
AUTHOR ADDRESS: (a)Div. Atherosclerosis, Nuitrition Lipid Research, Box 8046, 660 South Euclid Ave., St. Louis, MO **USA
JOURNAL: Journal of Clinical Investigation 99 (3):p424-432 1997
ISSN: 0021-9738
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Reactive aldehydes derived from reducing sugars and lipid peroxidation play a critical role in the formation of advanced glycation end (AGE) products and oxidative tissue damage. We have recently proposed another mechanism for aldehyde generation at sites of inflammation that involves myeloperoxidase, a heme enzyme secreted by activated phagocytes. We now demonstrate that human neutrophils employ the myeloperoxidase-H-2O-2-chloride system to produce alpha-hydroxy and alpha,beta-unsaturated aldehydes from hydroxy-amino acids in high yield. Identities of the aldehydes were established using mass spectrometry and high performance liquid chromatography. Activated neutrophils converted L-serine to glycolaldehyde, an alpha-hydroxyaldehyde which mediates protein cross-linking and formation of N-epsilon(carboxymethyl)lysine, an AGE product. L-Threonine was similarly oxidized to 2-hydroxypropanal and its dehydration product, acrolein, an extremely reactive alpha,beta-unsaturated aldehyde which **alkylates** proteins and **nucleic** acids. Aldehyde generation required neutrophil activation and a free hydroxy-amino acid; it was inhibited by catalase and heme poisons, implicating H-2O-2 and myeloperoxidase in the cellular reaction. Aldehyde production by purified myeloperoxidase required H-2O-2 and chloride, and was mimicked by reagent hypochlorous acid (HOCl) in the absence of enzyme, suggesting that the reaction pathway involves a chlorinated intermediate. Collectively, these results indicate that the myeloperoxidase-H-2O-2-chloride system of phagocytes converts free hydroxy-amino acids into highly reactive alpha-hydroxy and alpha,beta-unsaturated aldehydes. The generation of glycolaldehyde,

2-hydroxypropanal, and acrolein by activated phagocytes may thus play a role in AGE product formation and tissue damage at sites of inflammation.

1997

4/3,AB/26 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10072223 BIOSIS NO.: 199598527141
Evaluation by polymerase chain reaction on the effect of betapropiolactone and binary ethyleneimine on DNA.
AUTHOR: Groseil C; Guerin P; Adamowicz P(a)
AUTHOR ADDRESS: (a)Lab. Francais du Fractionnement et des Biotechnologies, 3 avenue des Tropiques, BP 305, 91958 Le**France
JOURNAL: Biologicals 23 (3):p213-220 1995
ISSN: 1045-1056
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Inactivating treatments for viruses such as pasteurization or **alkylation** by beta-propiolactone or binary ethyleneimine were tested for their capacity to modify **nucleic** acids. The modification of a **nucleic** acid was measured as the decrease in spot intensity in Southern blots after polymerase chain reaction (PCR) amplification. The inactivating treatments were applied to cellular and viral genomic material from a human lymphoblastoid cell line immortalized by Epstein Barr Virus (EBV), which produced a monoclonal antibody. Pasteurization did not modify the ability to amplify and detect cellular or viral DNA. Binary ethyleneimine strongly reduced the amount of detectable DNA and beta-propiolactone under particular conditions of incubation abolished all trace of DNA.

1995

4/3,AB/27 (Item 23 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09868143 BIOSIS NO.: 199598323061
A procedure for selective DNA **alkylation** and detection by mass spectrometry.
AUTHOR: Gut Vvo G(a)
AUTHOR ADDRESS: (a)DNA Sequencing Lab., Imperial Cancer Res. Fund, PO Box 123, 44 Lincoln's Inn Fields, London WC2A**UK
JOURNAL: Nucleic Acids Research 23 (8):p1367-1373 1995
ISSN: 0305-1048
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A method which improves the detectability of DNA by mass spectrometry is presented. By quantitatively **alkylating** the backbone of phosphorothioate oligonucleotides the problems of gas phase ion generation by matrix assisted laser desorption ionization can be controlled. We have developed a selective **alkylating** protocol for phosphorothioate oligonucleotides which is a facile way of generating non-ionic **nucleic** acids. A variety of **alkylating** agents was studied and their kinetics were monitored in a gel electrophoretic assay and by mass spectrometry.

1995

4/3,AB/28 (Item 24 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09468898 BIOSIS NO.: 199497477268
On the consistency between the electron density based bonding model for diazonium ions and experimental properties.
AUTHOR: Horan Christopher J; Glaser Rainer
AUTHOR ADDRESS: Dep. Chem., Univ. Mo., Columbia, MO 65211**USA
JOURNAL: Abstracts of Papers American Chemical Society 208 (1-2):pORGN 146 1994
CONFERENCE/MEETING: 208th National Meeting of the American Chemical Society Washington, D.C., USA August 21-25, 1994
ISSN: 0065-7727
RECORD TYPE: Citation
LANGUAGE: English
1994

4/3,AB/29 (Item 25 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09412395 BIOSIS NO.: 199497420765
The excretion of 7-methyladenine in the urine of rats exposed to carcinogenic methylating agents.
AUTHOR: Mandel H George(a); Straw James A; Wenger Laurie J; Kusmierz Jozef J
AUTHOR ADDRESS: (a)Dep. Pharmacol., George Washington Univ. Med. Cent., Washington, DC 20037**USA
JOURNAL: Carcinogenesis (Oxford) 15 (7):p1393-1398 1994
ISSN: 0143-3334
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Earlier studies showed that urine of rats which had been injected with the methlating agent N-(3H-methyl)-N-nitrosourea contained a previously undetected metabolic product, 7-(3H-methyl)adenine. This methylpurine, undoubtedly derived from **alkylation** of **nucleic** acids followed by depurination, was not labeled when 14C-methyl-labeled methionine was administered concurrently. To establish whether urinary 7-methyladenine (7-MA) might serve as a marker of exposure to exogenous and carcinogenic methylating agents, the excretion of 7-MA following injection of methylating agents was measured. A GC-MS method, using pentafluorobenzyl derivatives and an internal standard of tri-deutero-7-MA, was developed to assay levels of 7-MA. Increasing the i.p. dose of N-methylnitrosourea (MNU) from 2 to 80 mg/kg/rat resulted in a linear increase in urinary 7-MA, which at the highest dose was 1.6 mu-g during the first day and another 0.4 mu-g during day 2. Doses of 5 mg/kg MNU led to elevated urinary levels of 7-MA (144 ng) compared to controls (26 ng). Other methylating agents, such as dimethylnitrosamine, N-methyl-N'-nitro-N-nitrosoguanidine and dimethyl sulfate, also provided urinary 7-MA. To determine the fate of injected 7-MA, the administration of 2 mu-g 7-(3H-methyl)adenine led to an 80% recovery of radioactivity in the urine, almost all of it during the first 24 h. No other labeled metabolites were detected. At least for the rat, urinary 7-MA serves as an indicator of exposure to methylating agents.

1994

4/3,AB/30 (Item 26 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08904114 BIOSIS NO.: 199396055615
Structure, DNA minor groove binding, and base pair specificity of **alkyl**- and aryl-linked bis(amidinobenzimidazoles) and bis(amidinoindoles).
AUTHOR: Fairley Terri A; Tidwell Richard R; Donkor Isaac; Naiman Noreen A; Ohemeng Kwasi A; Lombardy Richard J; Bentley James A; Cory Michael(a)
AUTHOR ADDRESS: (a)Div. Org. Chem., Burroughs Wellcome Co., Research Triangle Park, NC 27709**USA
JOURNAL: Journal of Medicinal Chemistry 36 (12):p1746-1753 1993
ISSN: 0022-2623
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A series of bis(amidinobenzimidazoles) and bis(amidinoindoles) with varied linking chains connecting the aromatic groups and various modifications to the basic amidino groups have been prepared. The calf thymus (CT) DNA and **nucleic** acid homopolymer (poly(dA) cntdot poly(dT), poly(dA-dT) cntdot poly(dA-dT), and poly(dG-dC) cntdot poly(dG-dC)) binding properties of these compounds have been studied by thermal denaturation (DELTA-T-m) and viscosity. The compounds show a greater affinity for poly(dA) cntdot poly(dT) and poly(dA-dT) cntdot poly(dA-dT) than for poly(dG-dC) cntdot poly(dG-dC). Viscometric titrations indicate that the compounds do not bind by intercalation. Molecular modeling studies and the biophysical data suggest that the molecules bind to the minor groove of CT DNA and homopolymers. Analysis of the shape of the molecules is consistent with this mode of **nucleic** acid binding. Compounds with an even number of methylenes connecting the benzimidazole rings have a higher affinity for DNA than those with an odd number of methylenes. Molecular modeling calculations that determine the radius of curvature of four defined groups in the molecule show that the shape of the molecule, as a function of chain length, affects the strength of **nucleic** acid associated differential in **nucleic** acid base pair specificity or affinity.

1993

4/3,AB/31 (Item 27 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08808951 BIOSIS NO.: 199395098302
Bead-based sandwich hybridization characteristics of oligonucleotide-alkaline phosphatase conjugates and their potential for quantitating target RNA sequences.
AUTHOR: Ishii Jennifer K; Ghosh Soumitra S(a)
AUTHOR ADDRESS: (a)Life Sci. Res. Lab., Baxter Diagnostics Inc., 4245 Sorrento Valley Blvd., San Diego, CA 92121
JOURNAL: Bioconjugate Chemistry 4 (1):p34-41 1993
ISSN: 1043-1802
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The hybridization characteristics of oligonucleotide-alkaline phosphatase conjugate probes were examined in bead-based sandwich hybridization reactions using single-stranded **nucleic** acid targets and oligonucleotide-polystyrene capture beads. Enzymatic activity was

monitored using a chemiluminescent substrate and calibration plots of chemiluminescent signal versus conjugate concentration were used to estimate the sandwich hybridization efficiencies. Improved hybridization behavior was noted using glycerol as an additive and by increasing the length of the probe and **alkyl** spacer of the conjugates. The chemiluminescent assay is at least as sensitive as those employing 32P-labeled probes and can detect as little as 10-20 amol of target RNA. The linear relationship of chemiluminescent signal versus target assayed provides a method for quantitating unknown target samples. A single human immunodeficiency virus type 1 infected cell in a background of 10-6 unifnected cells is facilely detected when this enzyme-based detection assay is prefaced with a self-sustained sequence-replication amplification reaction.

1993

4/3,AB/32 (Item 28 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08792402 BIOSIS NO.: 199395081753
Distance distribution in a dye-linked oligonucleotide determined by time-resolved fluorescence energy transfer.
AUTHOR: Hochstrasser Remo A; Chen Shiow-Meei; Millar David P(a)
AUTHOR ADDRESS: (a)Scripps Res. Inst., Dep. Mol. Biol., MB20, 10666 N. Torrey Pines Rd., La Jolla, CA 92037**USA
JOURNAL: Biophysical Chemistry 45 (2):p133-141 1992
ISSN: 0301-4622
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Fluorescence energy transfer is potentially a useful technique for obtaining structural and dynamic information on duplex and branched DNA molecules suitably labeled with donor and acceptor days. We have assessed the accuracy and limitations of FET measurements in **nucleic** acids with respect to the localization of the dyes and the flexibility of the dye-DNA linkages. A nine base-pair duplex oligonucleotide was synthesized with donor and acceptor dyes linked at the opposing 5' termini by **alkyl** chains. A careful analysis of the fluorescence decay of the donor revealed that the donor-acceptor distance in this molecule was not well defined, but was described by a rather broad distribution. The mean donor-acceptor distance and the distribution of distances have been recovered from the donor decay. Orientational effects on energy transfer have been included in the analysis. The implications of these findings of FET measurements in **nucleic** acids are considered.

1992

4/3,AB/33 (Item 29 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08045459 BIOSIS NO.: 000093078807
4-4 NITROBENZYLPYRIDINE TESTS FOR **ALKYLATING** AGENTS FOLLOWING CHEMICAL OXIDATIVE ACTIVATION
AUTHOR: THOMAS J J; KIM J H; MAURO D M
AUTHOR ADDRESS: DEP. BIOL. SCI., FLA. INST. TECHNOL., MELBOURNE, FLA. 32901, USA.
JOURNAL: ARCH ENVIRON CONTAM TOXICOL 22 (2). 1992. 219-227. 1992
FULL JOURNAL NAME: Archives of Environmental Contamination and Toxicology

CODEN: AECTC
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A chemical activation system (CAS) designed to mimic the mammalian mixed-function oxidase enzymes was found to activate target compounds to reactive electrophiles. Activated compounds were assayed by reaction with 4-(4-nitrobenzyl)pyridine (NBP). A model nucleophile of 7-**alkylguanine** of **nucleic** acids, NBP produces a violet color following **alkylation**. Twenty compounds from several chemical classes were tested. The test generally gave positive and negative responses where expected. Two compounds, trichloroethylene and diethylnitrosamine, exhibited a linear Beer's law relationship in the concentration range tested. A high degree of linear correlation ($r > 0.97$) was obtained for these compounds. Other compounds showed varying degrees of linear correlation from high correlation ($r = 0.94$) to weak correlation ($r = 0.44$). The CAS-NBP assay results were compared to bacterial mutagenicity and animal carcinogenicity test results when information was available. A good correlation ($r = 0.80$) existed between direct **alkylating** activity and direct mutagenicity. Similar correlations existed between NBP **alkylation** following activation and mutagenicity following microsomal activation ($r = 0.73$). Also, different correlations were observed between carcinogenicity and NBP **alkylation** following activation ($r = 0.69$) and without activation ($r = 0.38$).

1992

4/3,AB/34 (Item 30 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06817667 BIOSIS NO.: 000088127112
APPLICATION OF SOFT-IONIZATION MASS SPECTROMETRY IN BIOCHEMISTRY
AUTHOR: SUKHODUB L F
AUTHOR ADDRESS: PHYS. TECH. INST. LOW TEMP., ACAD. SCI. UKR. SSR, KHARKOV, USSR.
JOURNAL: UKR BIOKHIM ZH 61 (4). 1989. 16-30. 1989
FULL JOURNAL NAME: Ukrainskii Biokhimicheskii Zhurnal
CODEN: UBZHD
RECORD TYPE: Abstract
LANGUAGE: RUSSIAN

ABSTRACT: Basic principles of mass spectrometry (MS) and methods of ionization are described. Methodological aspects of field ionization (FI) and field desorption (FD) MS are considered in detail. Examples are given demonstrating application of FI and FD MS as an **analytical** tool for structure analysis and identification of mono-, di- and oligosaccharides, **nucleic** acid bases, nucleosides, nucleotides, oligonucleotides, biomacromolecules (DNA, polysaccharides), microorganisms, metals in biological tissues and liquids, drugs (in particular, organophosphoric compounds) and their metabolites. The possibilites of fast atom bombardment MS in the investigation of dGuo and DNA **alkylation** by thiophosphamide are demonstrated.

1989

4/3,AB/35 (Item 31 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02353204 BIOSIS NO.: 000065010221

MACRO MOLECULAR COMPLEXES PRODUCED BY CHEMICAL CARCINOGENS AND UV RADIATION

AUTHOR: MORIN N R; ZELDIN P E; KUBINSKI Z O; BHATTACHARYA P K; KUBINSKI H
AUTHOR ADDRESS: MCARDLE LAB. CANCER RES., UNIV. WIS., MADISON, WIS. 53706, USA.

JOURNAL: CANCER RES 37 (10). 1977 3802-3814. 1977
FULL JOURNAL NAME: Cancer Research
CODEN: CNREA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effects of several carcinogenic and noncarcinogenic chemicals, UV light and some presumably noncarcinogenic analogs of carcinogenic compounds were tested for their ability to induce in vitro complexes between purified **nucleic** acids and **nucleic** acids and proteins. Several independent **analytical** methods were used to minimize the possibility of an unrecognized technical artifact. The results indicate that all of the ultimate tumor producing agents tested thus far fall into 2 distinct groups with respect to their ability to form macromolecular complexes. Class A of these chemicals includes several mono- and polyfunctional **alkylating** agents. **Nucleic** acid-**nucleic** acid and protein-**nucleic** acid adducts are produced in the presence of these compounds. Class B is exemplified by N-acetoxy-2-acetylaminofluorene, salts of Be and UV light. Complexes between proteins and **nucleic** acids, although not between the **nucleic** acids themselves, are produced in the presence of class B agents. Nonultimate carcinogenic chemicals such as N-hydroxy-2-acetylaminofluorene and 2-acetylaminofluorene do not give rise to any of these macromolecular complexs. They may be transformed into apparently active forms that then behave like class B carcinogens after exposure to mouse or rat liver extracts (postmitochondrial supernatants). None of the macromolecular complexes were produced by noncarcinogenic chemicals. Along with earlier observations, data reported in this paper indicate that a significant number and possibly all of the tumor producing agents are able to form macromolecular complexes. If such strong bonds between various chromosomal macromolecules are produced inside living cells exposed to carcinogenic agents, 1 extreme consequence of their formation may be nondisjunction of daughter chromosomes during mitosis and/or chromosomal breakdown. Such effects were often observed by others in tissues treated with carcinogens, and chromosomal aberrations are believed by some to correlate with malignant behavior.

1977